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CITATION:

YAMAGUCHI, YOSHIHIDE. Electron Microscopic Studies on the Experimental Cervical Myelopathy. 日本外科宝函 1980, 49(6): 713-738

ISSUE DATE:

1980-11-01

URL:

http://hdl.handle.net/2433/208485

Arch Jap Chir 49 (6), 713~738, Nov., 1980

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Electron Microscopic Studies on the Experimental Cervical Myelopathy

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Received for Publication, Sept. 8, 1980

To clarify the pathogenesis of cervical myelopathy, the fine structures of the cervical cord of rabbits given anterior compression with a screw were observed by electron microscopy. The animals were divided into three groups according to the degree of neurologic signs.

The first group showed no neurological deficit, the second showed symptoms of experimental cervical myelopathy, the third showed symptoms of acute spinal cord injury.

In the no deficit group, there were no degenerative changes in the nerve cells and axons in the cord. Slightly edematous changes were observed in the nerve fibers and capillaries. In the experimental myelopathy group the most striking observations were edematous changes in the microvasculature in the cord and degenerative changes in the myelinated nerve fibers. Though certain nerve cells had degenerative changes, they were slight.

In the acute cord injury group, the main findings were hemorrhage in the gray matter. Also severe damage was observed in the myelinated nerve fibers.

It was presumed from author's experimental results that cervical myelopathy might be produced by impairment of the conductive pathway due to axonal degeneration and edematous changes of the myelin sheaths, and also by the ischemic state of the spinal cord under edematous changes of capillaries.

Introduction

Cervical spondylotic myelopathy is the disorder based on degenerative changes of the cervical spine. Diagnosis and treatment of the myelopathy have been nearly established clinically.

But the pathogenesis of the myelopathy is still uncertain, though many experimental

Key words Cervical myelopathy, Spinal cord injury, Electron microscopy, Spinal cord, Edema.
索引語：頸髄症，脊髄損像，電子顕微鏡，脊髄，浮腫.
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studies on the pathogenesis have been performed mostly in the field of pathologic, micro-angiographic and biochemical observations of the cervical spine and the cervical spinal cord. Up to now two main factors regarding the pathogenesis have been proposed.[9,11,12,21,28,41] One is a mechanical factor, in which posterior spur or instability of the intervertebral space gives direct compression to the spinal cord usually under developmental canal stenosis[34]. The other one is a vascular factor, in which vascular insufficiency of the spinal cord such as ischemia or venous congestion is thought to play an important role for the myelopathy[8,9,10,29,42].

Many experimental studies on the pathogenesis of cervical myelopathy were performed in our clinic and the results were reported up to now[11,12,13,14,26,27,37]. However, electron microscopic study of the myelopathy has not been reported.

The main purpose of this paper is to clarify the pathogenesis of the cervical myelopathy in the field of fine structure of the cervical cord using electron microscope. Experimental cervical mylopathy is made on rabbits for the materials.

There have been a few papers regarding the fine alteration of morphology of the spinal cord following acute cord injury or transient paraplegia. But little is known on the fine alteration of the spinal cord in exprimental cervical myelopathy.

Materials and method

Forty nine white adult rabbits of both sexes, ranging in weight from 2.5 to 3.0 kg were used for this study. Under intravenous anesthesia of pentobarbital (30 mg/kg), a screw (3.6 mm diameter) was applied slowly into the C_{4-5} disc space through an anterolateral approach to the cervical spine in order to get anterior compression of the cervical cord. The tip of the screw was flattened by a rasp and the screws of various length were preliminarily arranged. After taking lateral and anteroposterior roentogenograms of the cervical spine, the animals were divided into four groups according to the compression ratio of the cord observed by how much the screw was placed into the spinal canal (Fig. 1). A compression ratio of less than 10% (10 animals) was group I, 11-30% (9 animals) was group II, 31-50% (15 animals) was group III, and more than 51% (5 animals) was group IV. 10 animals without operation were used as controls (Table 1).

The animals were followed up clinically for one, three, and six months after the operation for each group, with evaluations of walking, motor function of the limbs, and examination of the deep tendon reflexes. The evaluations were performed initially on a daily and then at weekly intervals. If the animal showed tetraplegia and incontience of urine and stool immediately after the operation, and these symptoms did not recover at all, the author classified these symptoms as an acute spinal cord injury. If the animal showed no neurological deficit after the operation, but some days later gradually exhibited unstable and spastic gait, motor weakness of the limbs, and hyperreflexia of the deep tendons, the author classified these symptoms as an experimental cervical myelopathy.

The animals in an experimental cervical myelopathy and acute spinal cord injury were

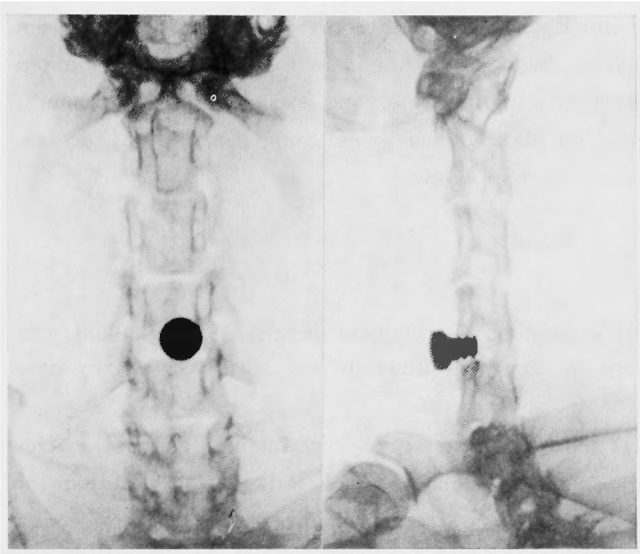


Fig. 1 The anterior compression operations to the cervical spine were performed slowly with a screw through an anteroloateral approach. After taking lateral and anteroposterior roentogenograms, the animals were divided into four groups according to the compression ratio.

Table 1 Group of compression ratio and number of experimental animal

Group	Compression ratio (%)	Number of rabbit
I	10	10
II	11-30	9
III	31-50	15
IV	51	5

also killed within a few days after the appearance of neurological signs for the study of electron microscopy of the cervical cord.

All the animals without any cord symptoms were killed at one, three and six months after the operation for the study of electron microscope of the cervical cord.

They were perfused with 3% glutalaldehyde through a cannula in the abdominal aorta. Cervical laminectomy and a midline dural incision were performed as quickly as possible and three specimens of the cervical cord were excised with a razor-blade at the site of compression (C_{4-5}), the rostral segment (C_{3-4}) and the caudal segment (C_{5-6}). These segments were identified by tracing the corresponding nerve roots to the intervertebral foramen.

Each specimen was cut into pieces. Five pieces from the central and the peripheral portion of the gray matter and the anterior, the posterior and the lateral portion of the white matter were used for this study. Double postfixation in a 1% glutalaldehyde and a 1% osmium for 2 hours were performed and then they were dehydrated through graded

alcohols (50—100%), and embedded in Epon 812. Sections were cut on a Porter-B-um MT-1 ultra microtome with glass knives. Sections of 0.5mm in thickness were mounted on glass for microscope slides, stained with toluidine blue, and examined by light microscopy. Ultrathin sections were mounted on plain copper grids, stained with uranyl acetate and lead citrate, and examined in a electron microscope.

Results

1. *Clinical results* :

All the animals in group I and II showed no neurological deficit. They walked, ran and jumped normally, and no urinary or bowel dysfunction was observed at any time during the observation period.

Six of fifteen animals in group III showed symptoms of experimental cervical myelopathy. They recovered from anesthesia after the operation and walked, ran and jumped normally for several days. But, on the 14th to 42th days after the operation, they began to show unstable and spastic gait, motor weakness of the limbs, and hyperreflexia of the deep tendons. Sensory disturbance was examined with pinprick, but it was unreliable. These sympotoms seem to resemble human cervical spondylotic myelopathy. The remaining nine animals in group III showed no neurological deficit throughout the observation period.

All of the animals in group IV showed symptoms of acute spinal cord injury. They could not move or stand immediately after the operation, and incontinence of urine and stool was observed; moreover these animals did not recover at all.

According to clinical results during the observation period, all animals were divided into three groups; these are a no-deficit group, a myelopathy group, and a cord injury group. There were 28 animals in a no-deficit group, 6 in a myelopathy group, 5 in a cord injury group and 10 in a control group.

2. *Electron microscopic findings;*

1) control group

Fine structures of the gray matter and the white matter in the spinal cord of the control animals differed. Capillaries and cellular components (nerve cells, glial cells and glial processes) were rich in the gray matter, but were scanty in the white matter. The nerve cells of the spinal cord had a large nucleus with a very large nucleolus of high electron density. The nuclear membrane was of irregular contour and composed of two well defined layers.

Lateral ramifying processes or dendrites arose from the cell body (Fig. 2). The cytoplasm was characterized by prominent development of the rough endoplasmic reticulum, which consisted of dilated cisternae of various calibers and numerous ribosomes. The mitochondria and the Golgi complex were scattered here and there in the cytoplasm (Fig. 3). The blood vessels of the spinal cord were similar to those of other organs. Capillaries were composed of attenuated non fenestrated endothelium, enveloped by a basement

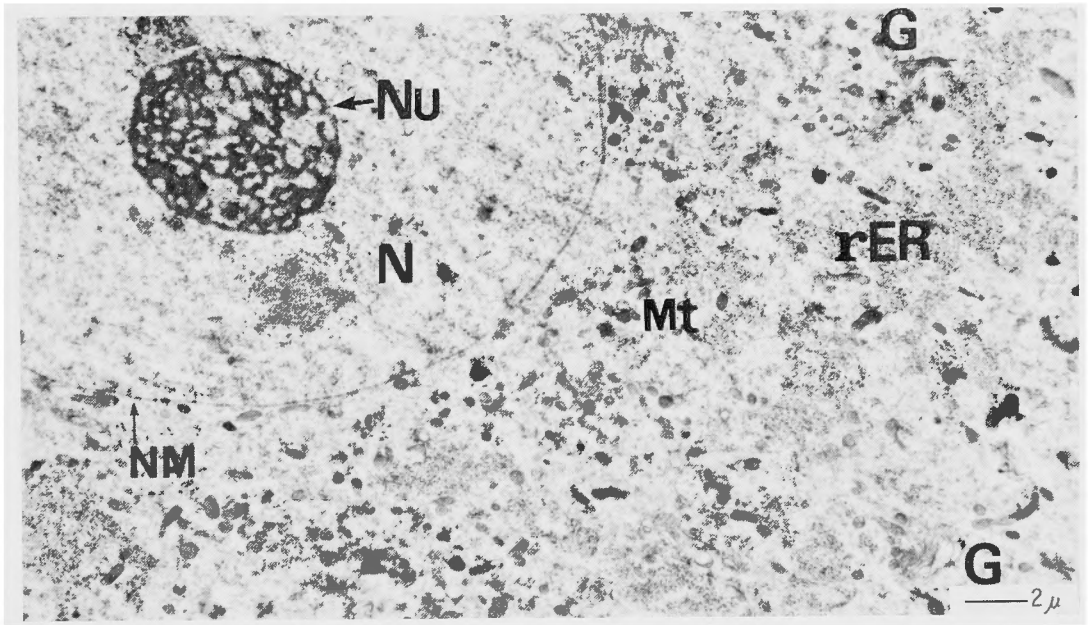


Fig. 2 Electron micrograph of the normal nerve cell within the gray matter in a control rabbit. nucleus (N) ; nucleolus (Nu) ; Golgi complex (G) ; mitochondria (MT) ; rough endoplasmic reticulum (rER) ; nuclear membrane (NM)

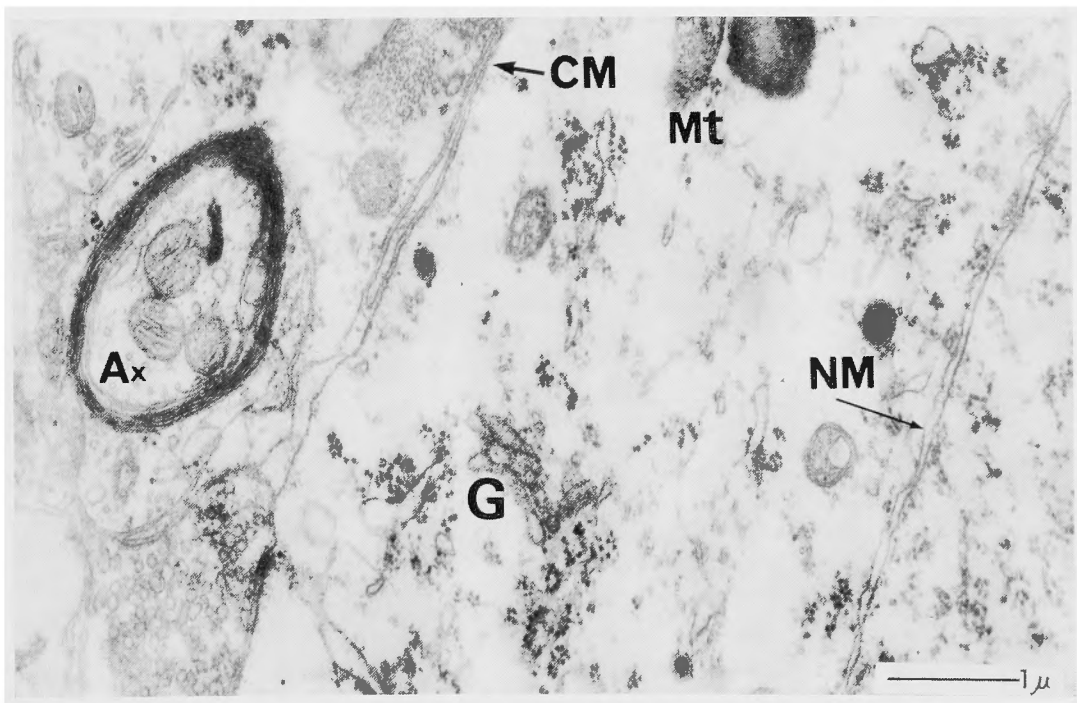


Fig. 3 Electron micrograph of the normal nerve cell and its surrounding structure. nuclear membrane (NM) ; Golgi complex (G) ; mitochondria (Mt) ; axon (Ax) ; cytoplasmic membrane (CM)

membrane. A pericyte was occasionally seen in the substance of the basement membrane. Basement membrane consitsted of a dense layer and bilateral lamina rase. A perivascular space, delimited by a glial basement membrane containing collagen fibrils and cytoplasmic processes, was around the arterioles. Glial processes, so called "perivascular feet", were jextaposed to the capillary basement membrane. Therefore, no perivascular space was present around the capillaries (Fig. 4). White matter contained a lot of myelinated nerve fibers enclosed in myelin lamellae of various thickness, however, cellular components and blood vessels were poor. Myelinated nerve fibers of lamellar structure consisted of myelin sheaths and axons, no periaxonal space between the axon and the circumjacent myelin was present (Fig. 5, 6).

2) no deficit group

Fine structures of both the gray matter and the white matter in group I resembled thcse of control animals. Capillaries, nerve cells and myelinated nerve firvers in both the gray matter and the white matter were of normal morphology (Fig. 7, 8). Morphological findings in 1, 3 or 6 months of group I were similar, and the difference of findings due to the length of observation period was not revealed.

In group II, slightly enlarged periaxonal spaces and separation of myelin sheaths were

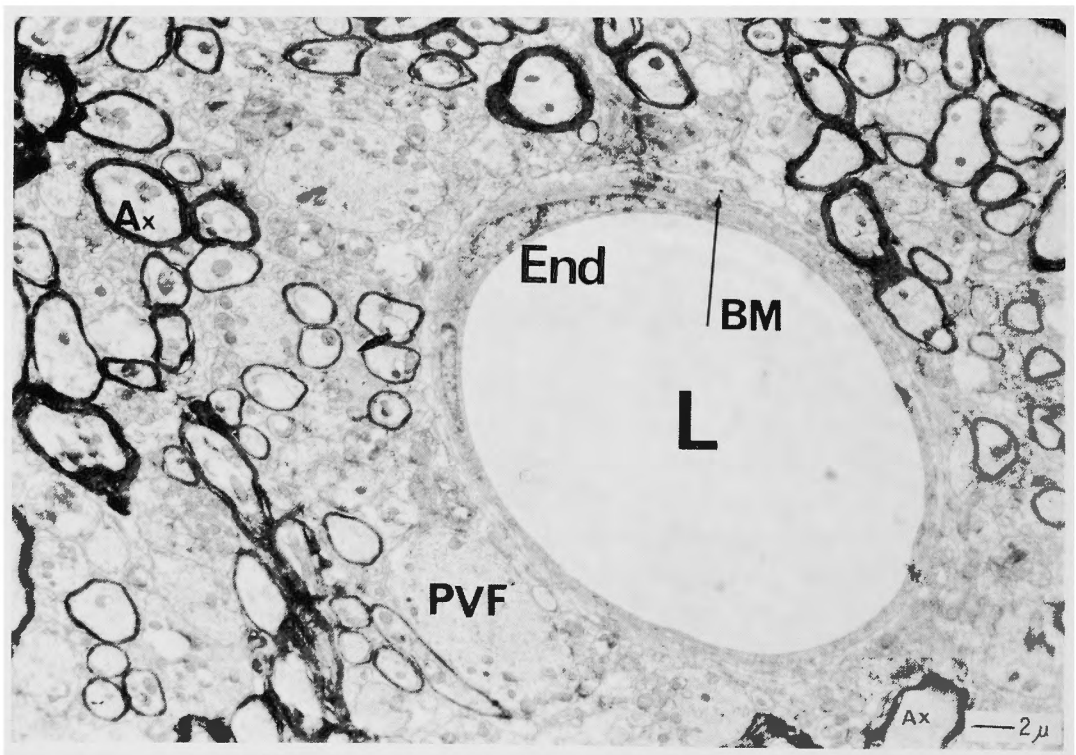


Fig. 4 Electron micrograph of the normal capillary in a control rabbit.
lumen (L) ; endothelial cell (End) ; basement membrane (BM);
axon (Ax) ; perivascular feet (PVF)

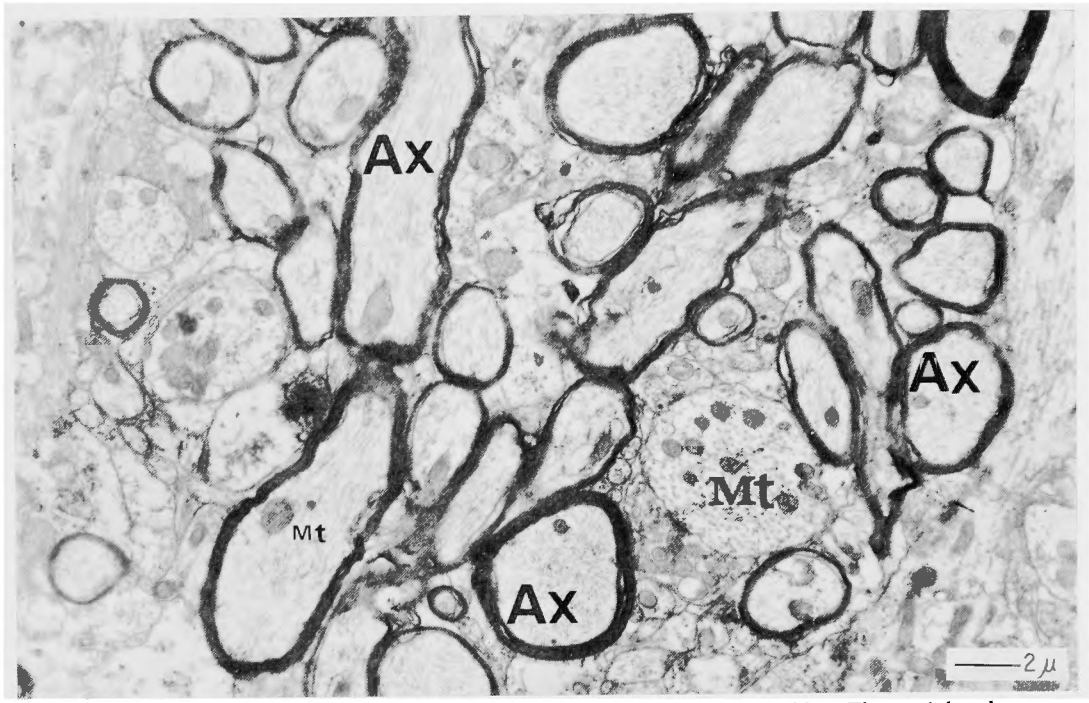


Fig. 5 Electron micrograph of the peripheral gray matter in a control rabbit. The peripheral gray matter are filled with the immature myelinated nerve fibers.
axon (Ax) ; mitochondria (Mt)

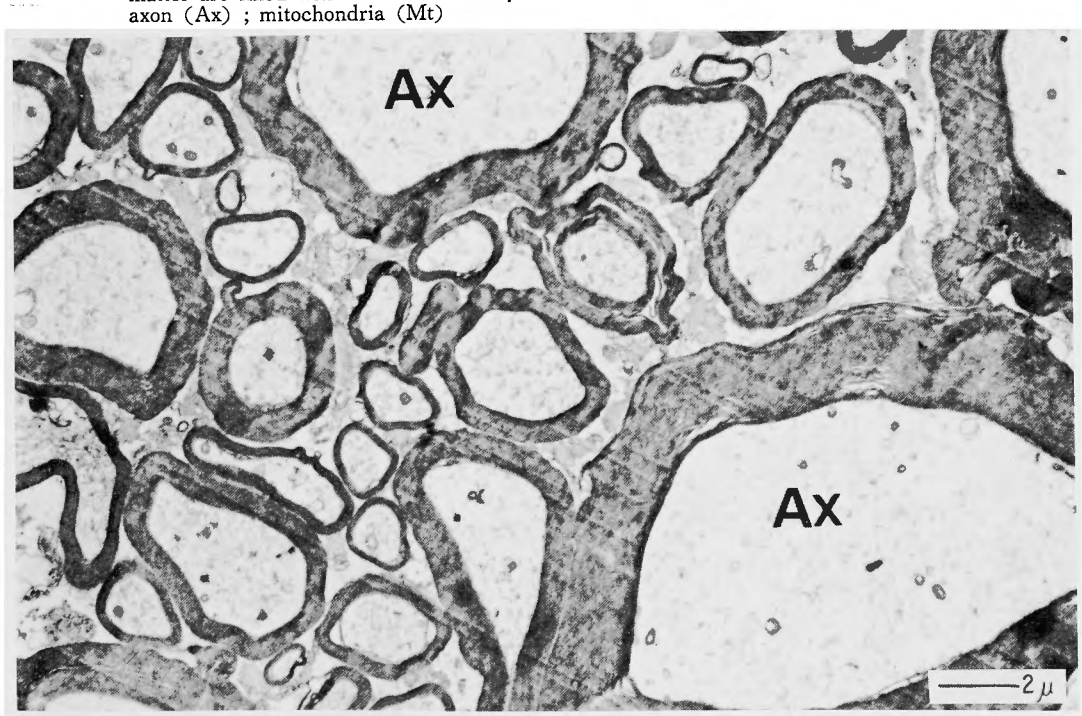


Fig. 6 Electron micrograph of the normal myelinated nerve fibers within the white matter in a control rabbit.
axon (Ax)

Fig. 7 Electron micrograph of the gray matter at 6 month post-compression in group Ⅰ. Capillary and myelinated nerve fibers are not altered.
lumen (L) ; endothelial cell (End) ; axon (Ax)

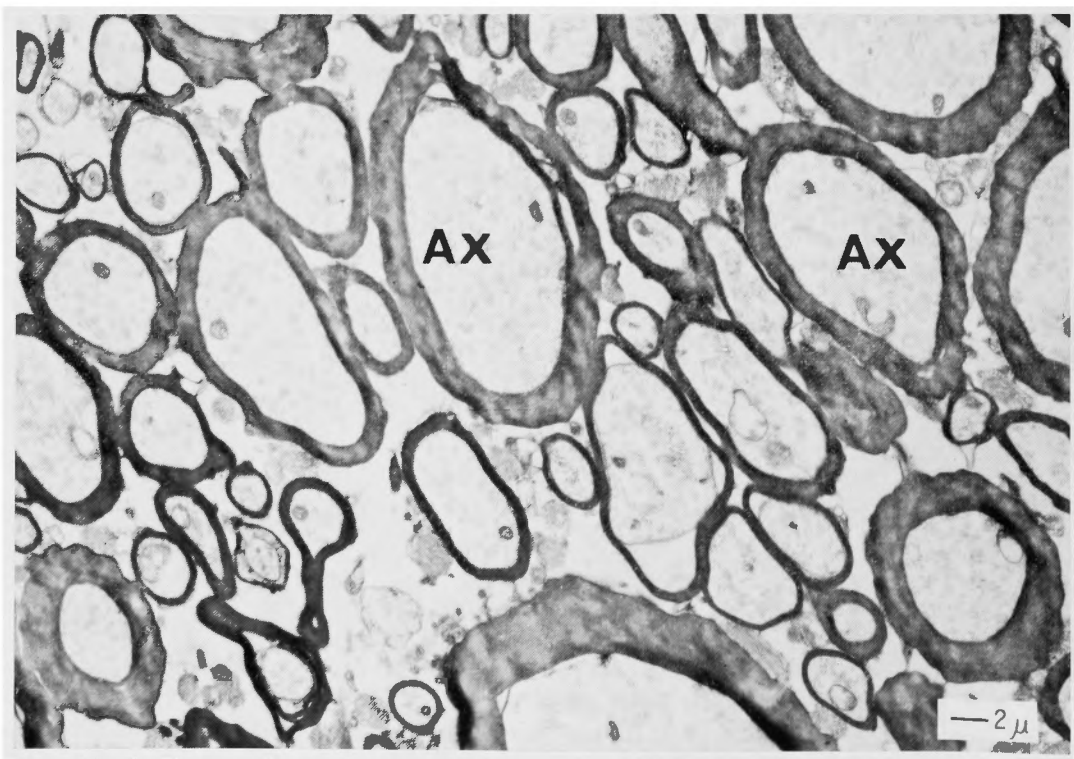


Fig. 8 Electron micrograph of the white matter at 6 months post-compression in group Ⅰ. Myelinated nerve fibers are of normal morphology.
axon (Ax)

noted in certain myelinated nerve fibers in the white matter. In general, however, no particular alternations in the fine structures of the myelin sheath or axons were present (Fig. 9). At 6 months, the findings of capillaries showed slight enlargement of the basement membrane (Fig. 10). Fine structure of nerve cells in the gray matter resembled those of the control group (Fig. 11).

In group III of no deficit group, vacuolar degeneration of nerve cells, enlargement of the basement membrane in capillaries and swelling of the perivascular feet were observed (Fig. 12, 13). Separation of the myelin sheaths and enlargement of the periaxonal space were progressed in group III (no deficit group) compared with group II. Separation of the myelin sheaths were particulary remarkable at 6 months in group III (no deficit group) (Fig. 14, 15).

3) myelopathy group

In the myelopathy group the fine structures of the nerve cells in the gray matter were altered. There were findings of pyknotic nucleus, irregular nucleus membrane, watery and edematous mitochondria, and degeneration of the endoplasmic reticulum (Fig.16).

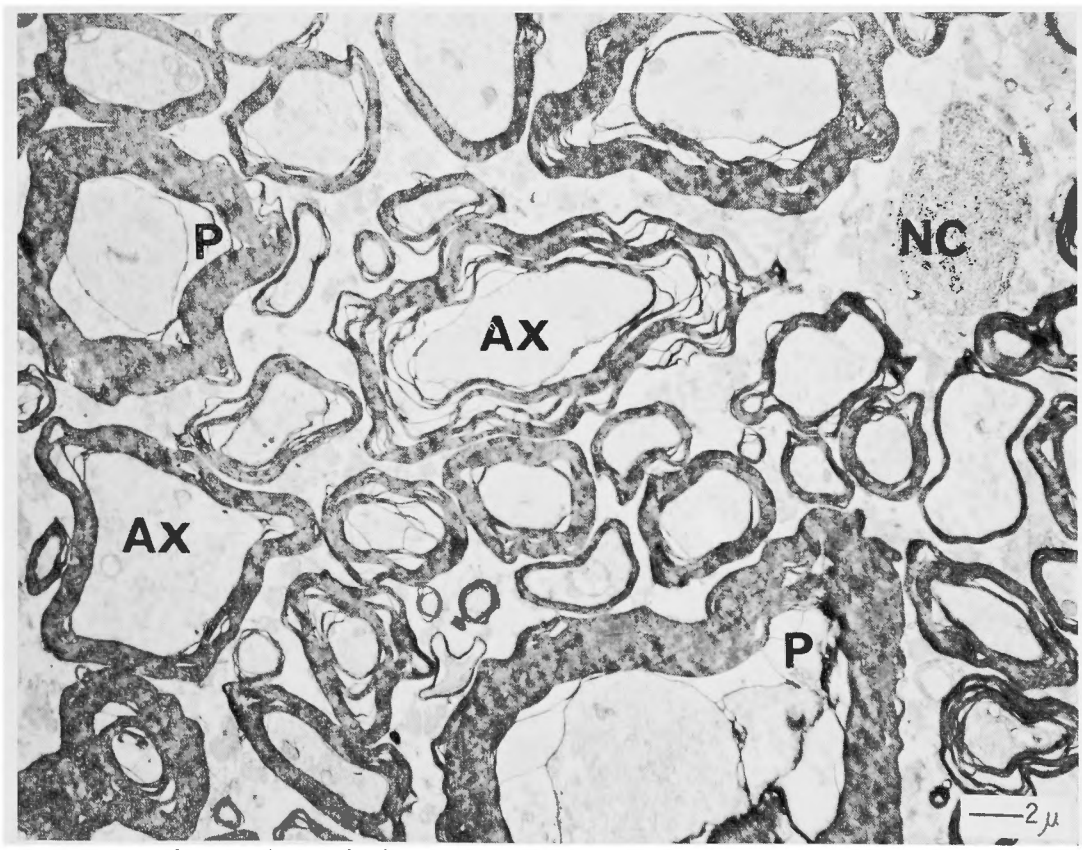


Fig. 9 Electron micrograph of the white matter at 3 months post-compression in group II. In this myelinated nerve fibers the periaxonal space (P) are enlarged slightly. axon (Ax) ; nerve cell (NC)

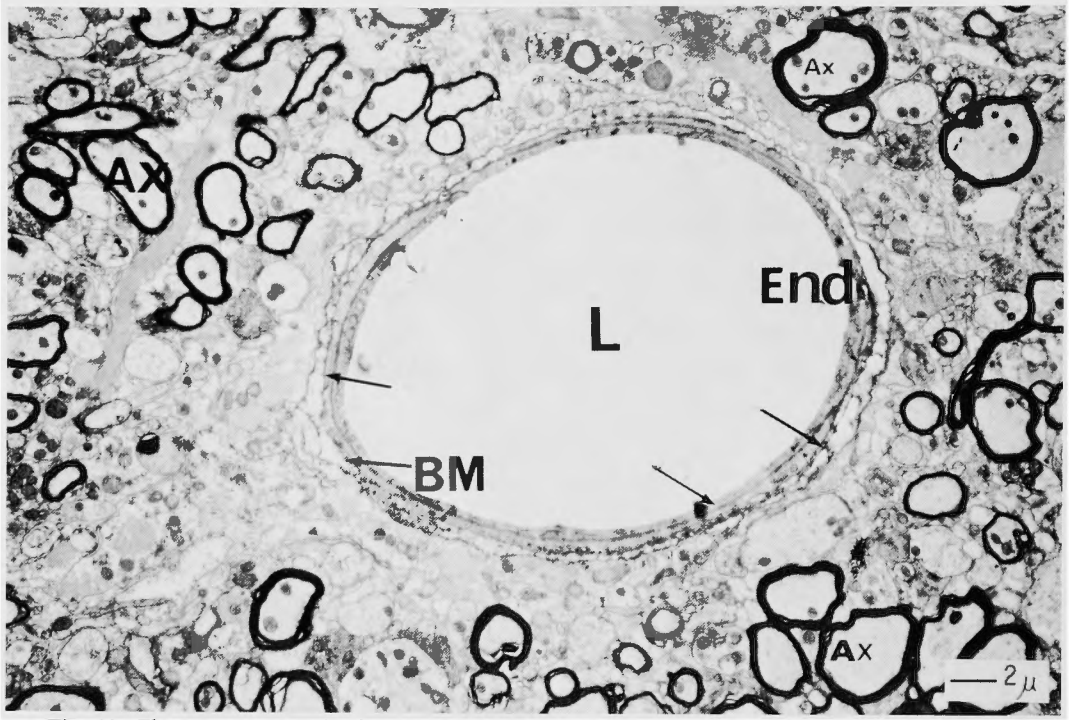


Fig. 10 Electron micrograph of the gray matter at 6 months post-compression in group II. The basement membrane (BM) of capillary is enlarged slightly. (arrows)
lumen (L) ; endothelial cell (End) ; axon (Ax)

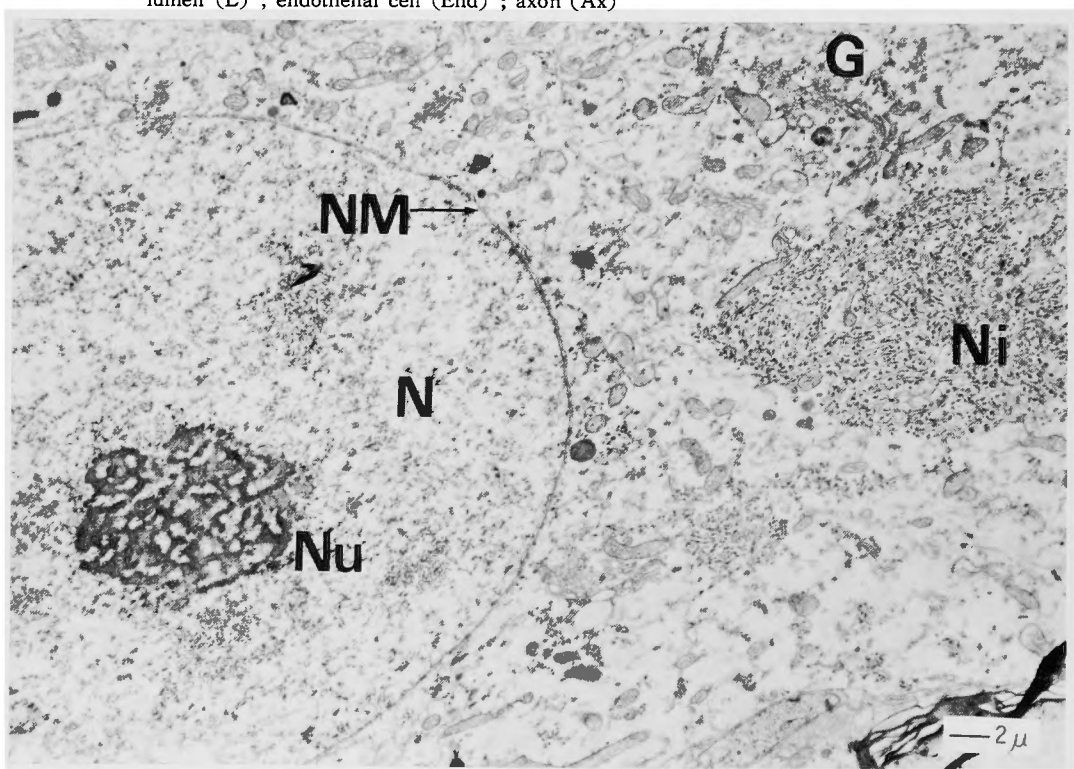


Fig. 11 Electron micrograph of the nerve cell at 6 months post-compression in group II. The fine structure of nerve cell is not altered.
nucleus (N) ; nucleolus (Nu) ; Golgi complex (G) ; Nissl's body (Ni) ; nuclear membrane (NM)

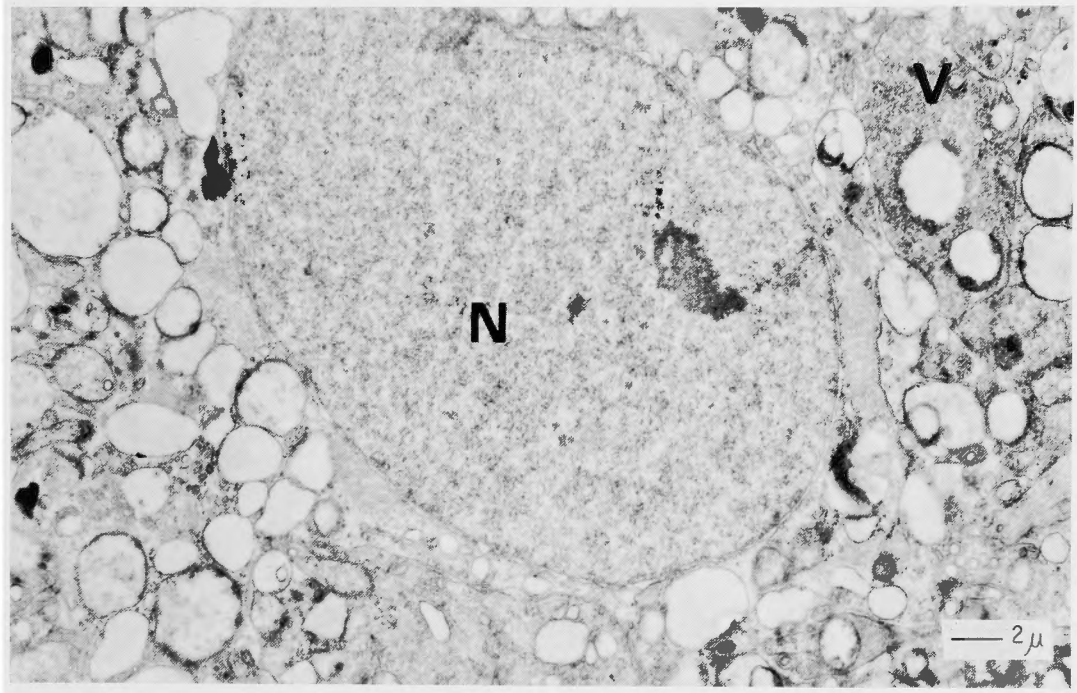


Fig. 12 Electron micrograph of the gray matter at 6 months post-compression in group III. Swelling of the numerous glial processes is seen, however, the nerve cell is not altered.
nucleus (N) ; vesicle (V)

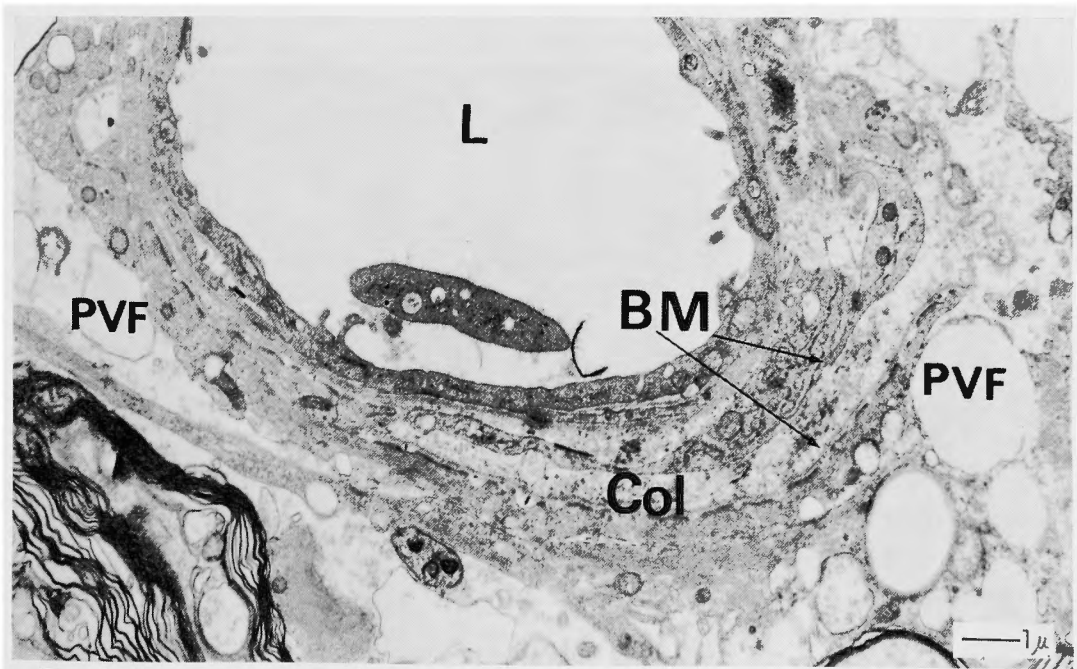


Fig. 13 Electron micrograph of the gray matter at 6 months post-compression in group III. The enlarged basement membrane (BM) and appearance of the collagen fibrils (Col) are showed in this capillary.
lumen (L) ; perivascular feet (PVF)

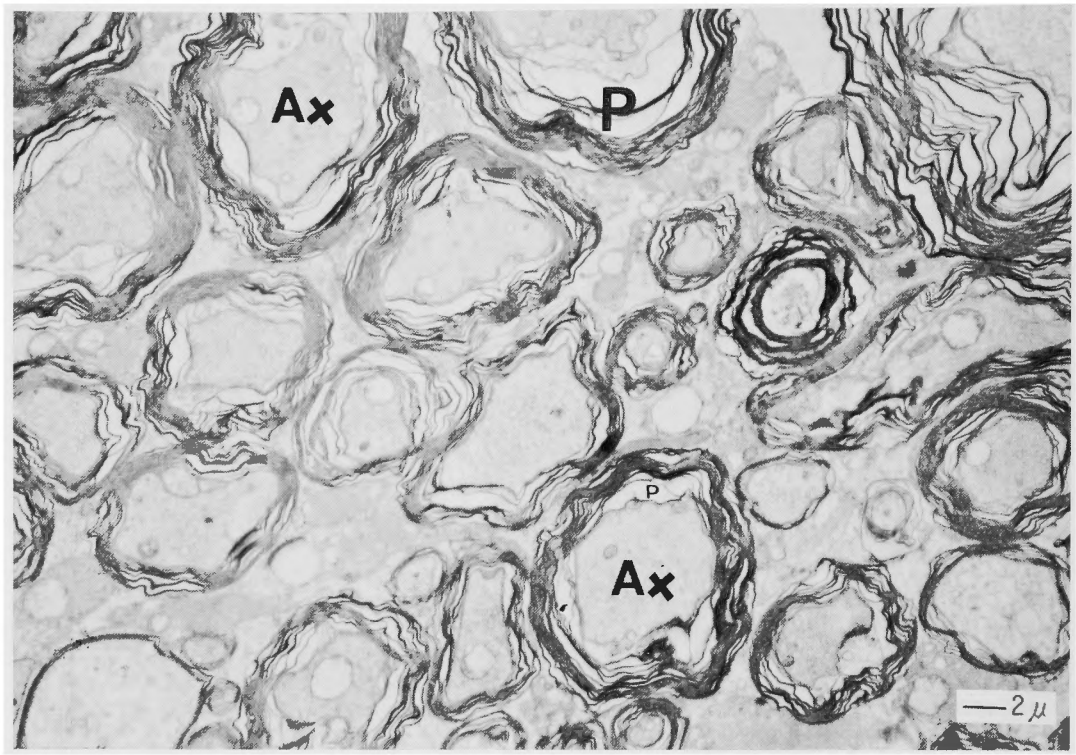


Fig. 14 Electron micrograph of the white matter at 3 months post-compression in group III. Enlargement of the periaxonal space (P) and separation of the myelin lamellae are showed, however, the axon (Ax) is not altered.

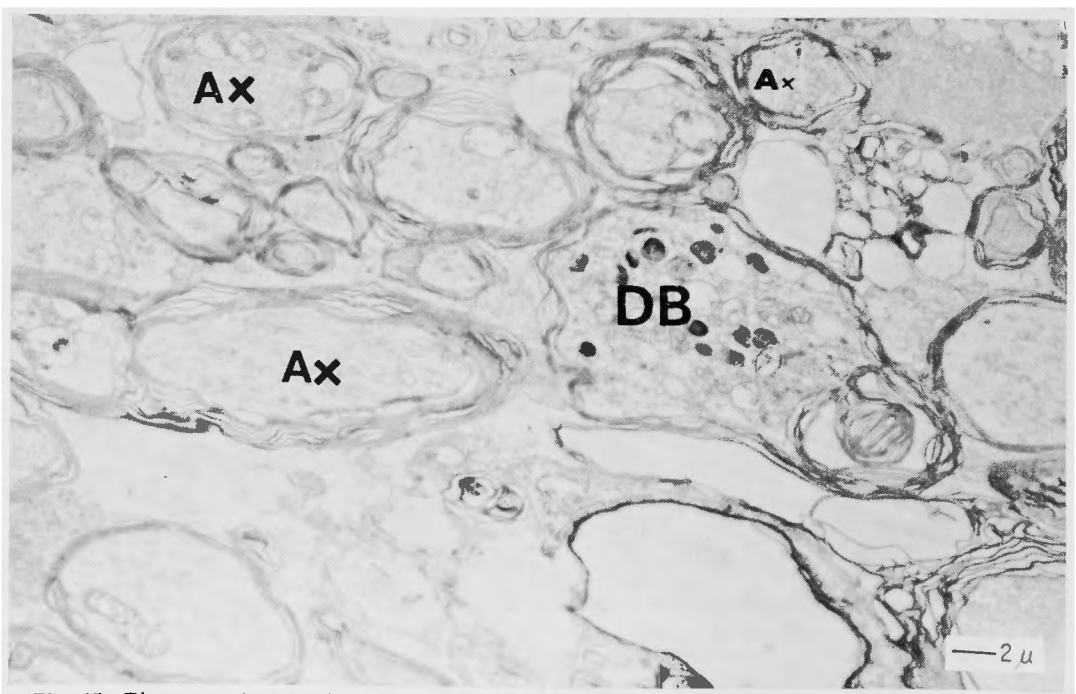


Fig. 15 Electron micrograph of the white matter at 6 months post-compression in group III. The myelinated nerve fibers are attenuated and the dense bodies (DB) appear in axon (Ax).

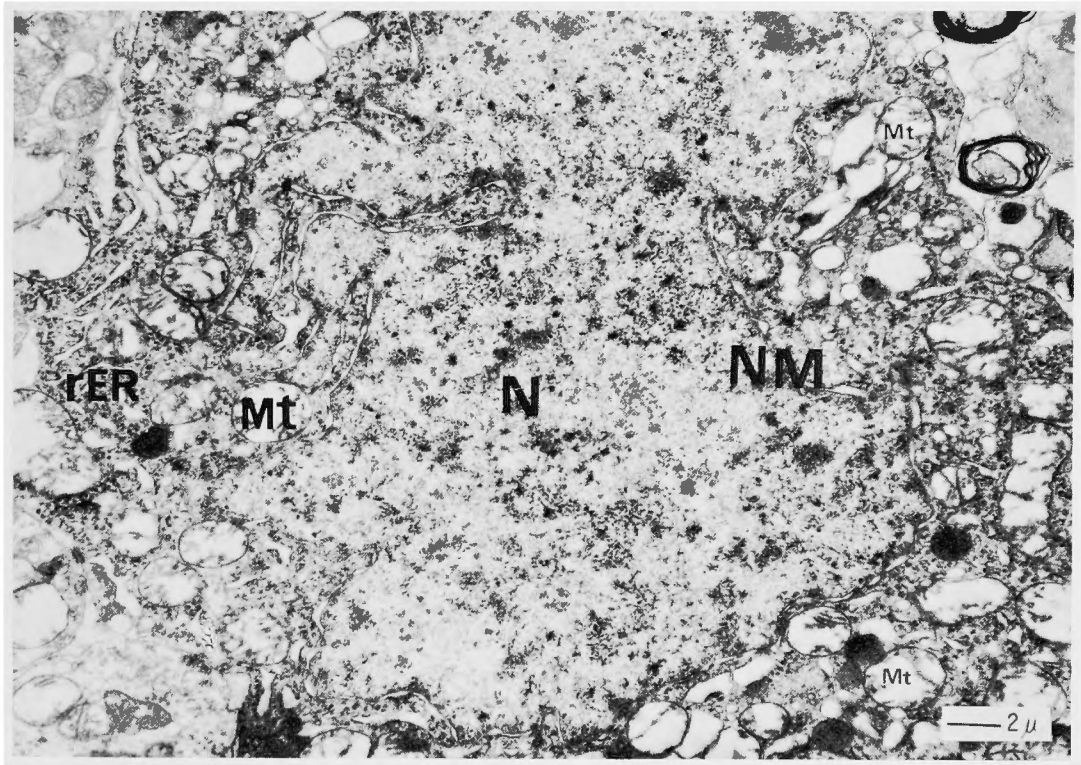


Fig. 16 Electron micrograph of the gray matter in myelopathy group. The nucleus membrane (NM) is irregular, swelling of mitochondria (Mt) and degeneration of the rough endoplasmic reticulum (rER) are seen.
nucleus (N)

Also degeneration of endoplasmic reticulum, mitochondria and synaptic vesicle was well observed (Fig. 17). Attenuation of the myelin sheath, dilatation of the periaxonal spaces, increase of the dense bodies, and apparent concentration of the axoplasm of some axons were the main morphological changes in the affected nerve fibers. These alterations were mainly noted in the white matter (Fig. 18, 19). Many capillaries in the gray matter showed narrowing of the lumen, and very increased collagen fibrils among the enlarged basement membranes, indicating edematous changes of capillaries. These edematous changes of capillaries caused significant reduction in the lumen. Mild swelling of astrocytic processes was present around capillaries of the gray matter (Fig. 20, 21).

In the myelopathy group the alterations in the rostral and the caudal segments were compared. The edematous changes and axonal regenerations in the affected nerve fibers were stronger in the caudal segment than in the rostral segment, although there was no difference of the alterations in the nerve cells and capillaries between them (Fig. 22, 23).

4) cord injury group

In the acute spinal cord injury, disruption of the glial basement membrane and consequent escape of erythrocytes from the perivascular spaces occurred in the gray matter

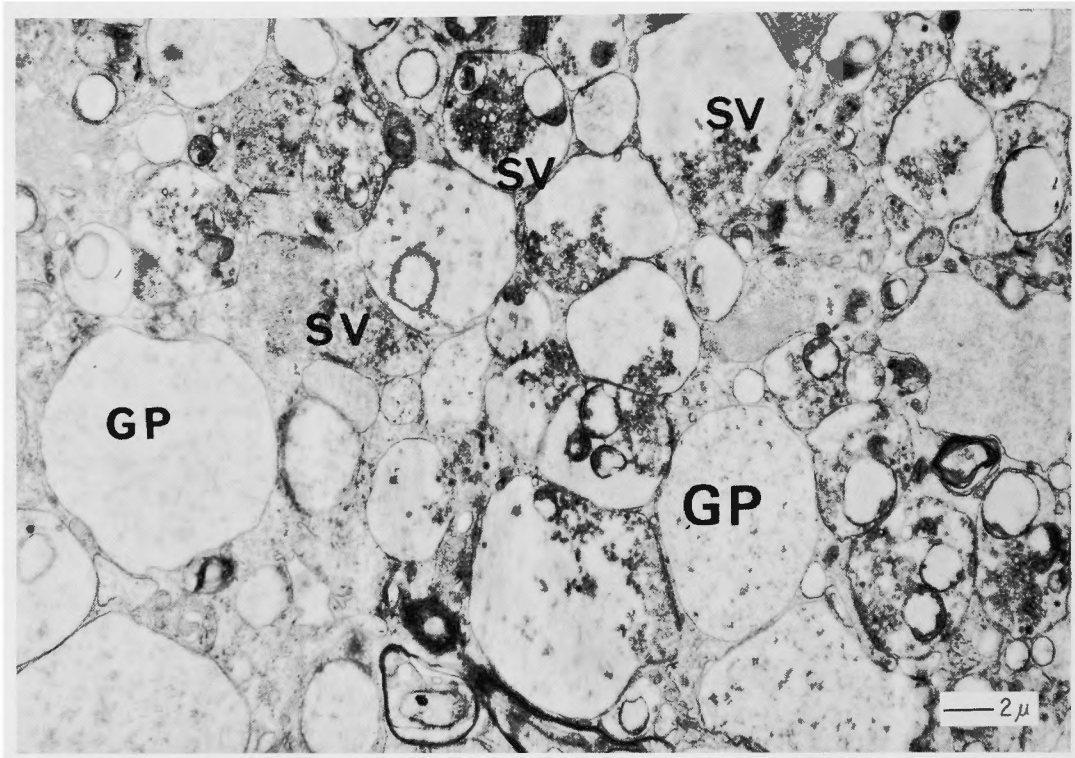


Fig. 17 Electron micrograph of the gray matter in myelopathy group. The glial processes (GP) are swollen and the synaptic vesicles (SV) are collected in the perivascular feet.

(Fig. 24). Also infiltration of neutrophiles was observed in certain areas (Fig. 25). Great numbers of erythrocytes were present in the gray matter and in certain areas of the white matter. The endothelium of capillaries showed vacuole formation and endothelial swelling. Predominantly the lumen of capillaries was irregular and narrow, and perivascular spaces were edematous (Fig. 26). In myelinated nerve fibers periaxonal space was greatly dilated and the myelin sheath was attenuated. Certain myelin sheaths showed splaying of their lamellae, while other sheaths were broken, leaving partially denuded axons (Fig. 27). Occasionally the degenerated axons were phagocyted by a macrophage (Fig. 28). The hemorrhage in the gray matter were extended to the rostral and caudal site, but there was no difference between them.

Discussion

With use of the apparatus of ALLEN[1] and ALBIN[2], many experimental studies have described of the hystopathology and pial circulation in the mammalian spinal cord following acute injury. There was most of the information regarding the alterations of spinal cord morphology following trauma[3,4,5,38,40,42,43].

But little is known of the fine structual alterations observed by electron microscope on the chronically compressed cervical spinal cord.

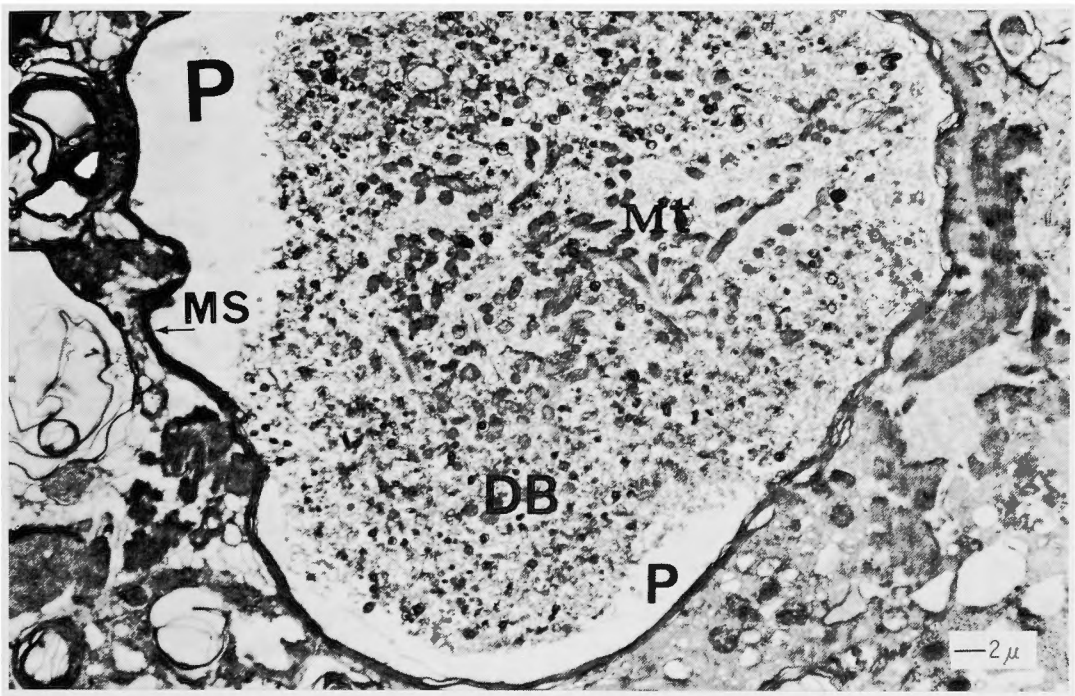


Fig. 18 Electron micrograph of the myelinated nerve fibers in myelopathy group. Showing the findings of attenuation of the myelin sheath (MS), dilation of the periaxonal space (P) and increase of the dense bodies (DB). mitochondria (Mt)

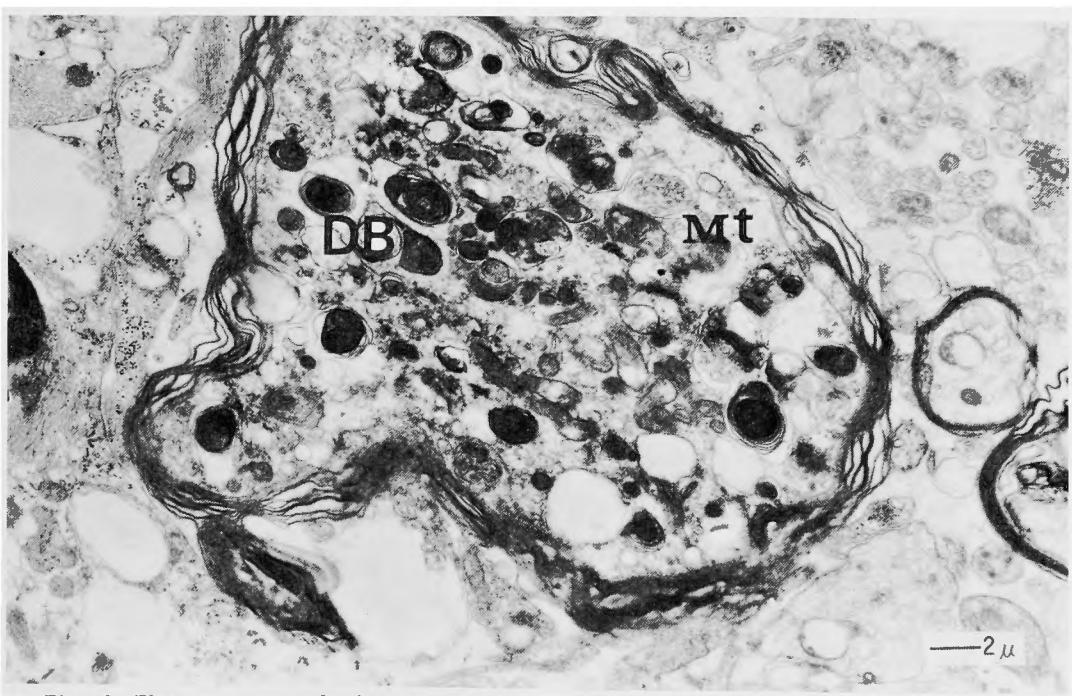


Fig. 19 Electron micrograph of the myelinated nerve fibers in myelopathy group. Attenuation and separation of the myelin sheath, and increase of the dense bodies (DB) are seen. The mitochondrias (Mt) in axon are disintegrated.

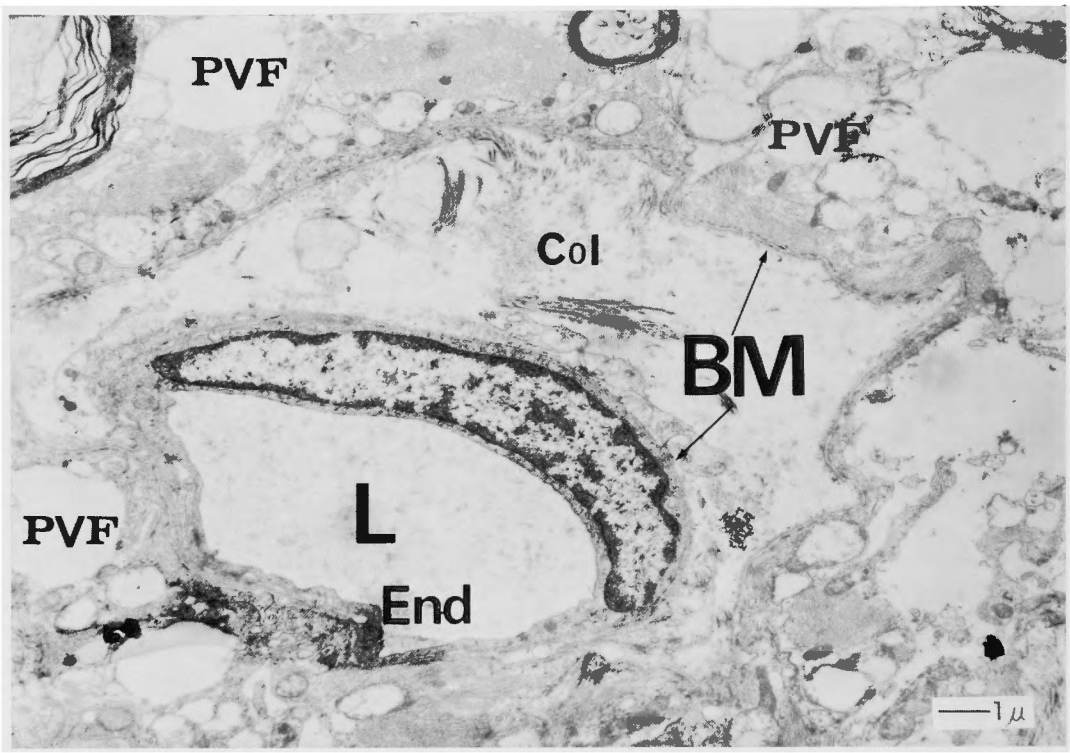


Fig. 20 Electron micrograph of the capillary in myelopathy group. Showing the narrowing of the lumen (L) and swelling of the perivascular feet (PVF). The collagen fibrils (Col) between the enlarged basement membrane (BM) are increased greatly.
endothelial cell (End)

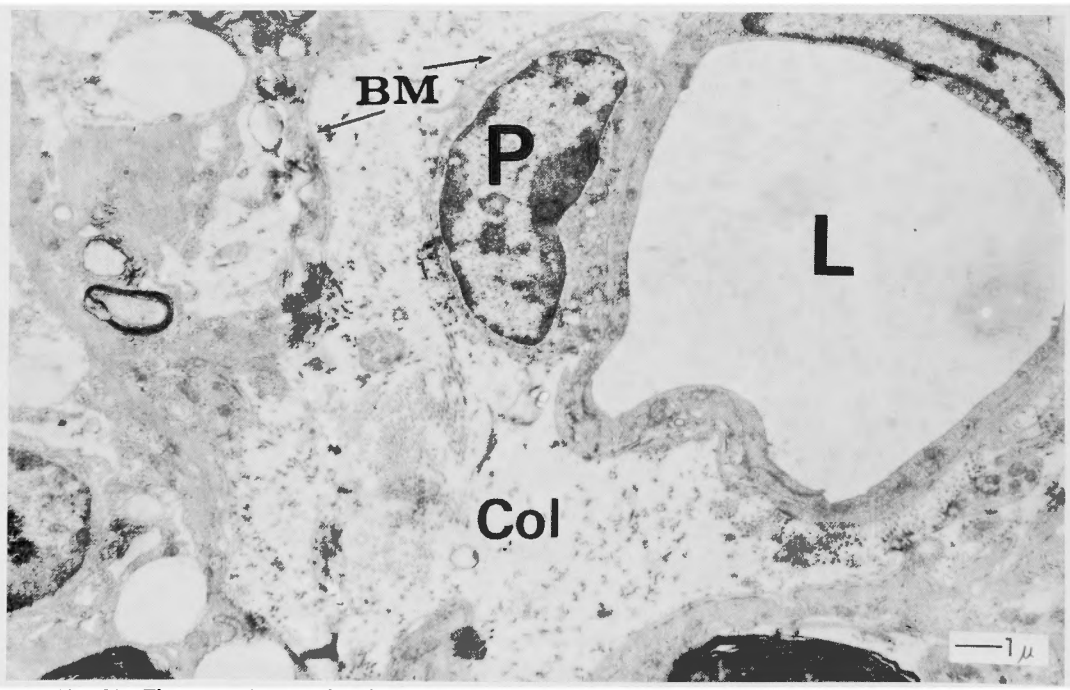
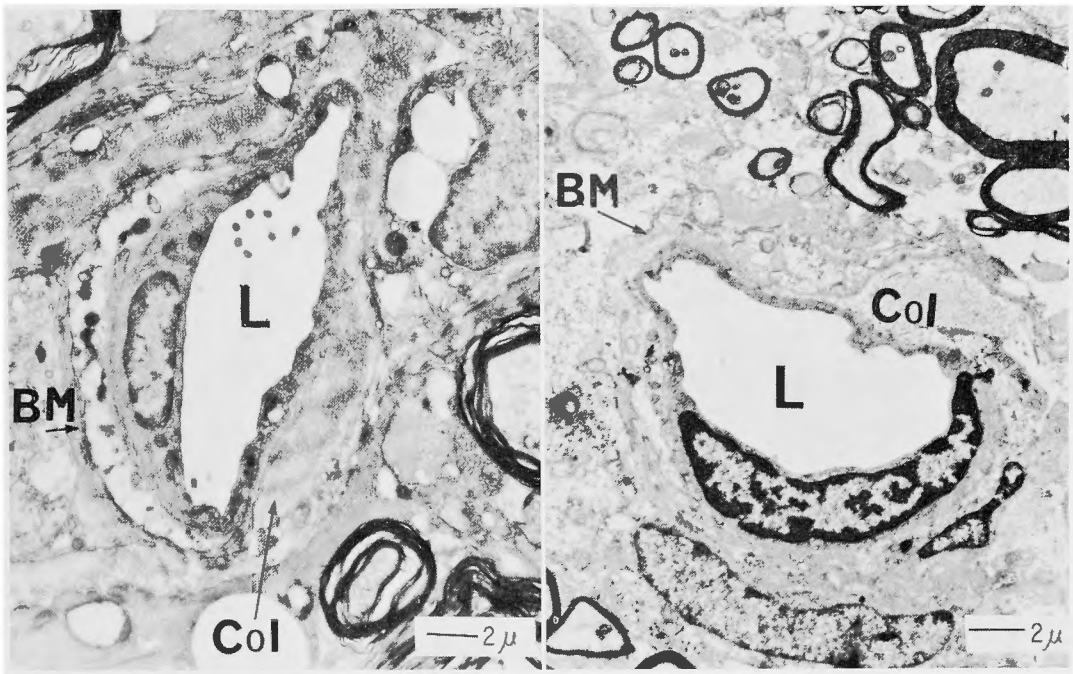
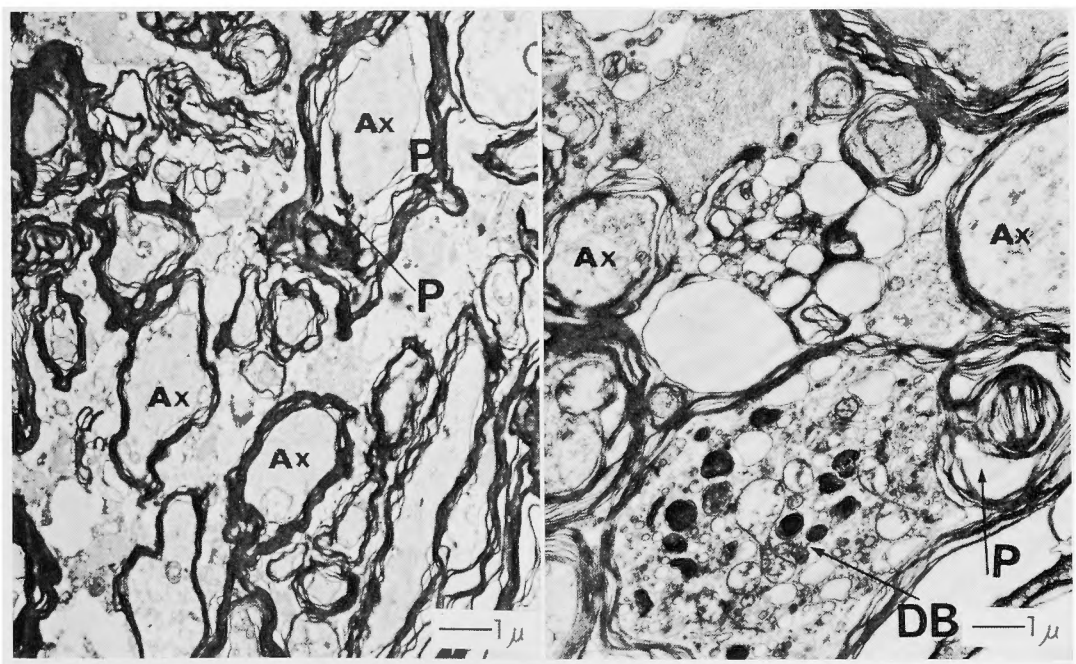


Fig. 21 Electron micrograph of the capillary in myelopathy group. The collagen fibrils (Col) between the enlarged basement membranes (BM) are increased greatly.
pericyte (P) ; lumen (L)



rostral caudal

Fig. 22 Electron micrograph of the capillary compared with in the rostral and caudal segment in myelopathy group. The collagen fibrils (Col) between the basement membranes (BM) are increased in the both, however, there is no difference of the alteration in the both. lumen (L)



rostral caudal

Fig. 23 Electron micrograph of the meylinated nerve fibers, compared with in the rostral and caudal segment in myelopathy group. There is no difference of the attenuation of myelin sheaths and the enlargement of the periaxonal space (P) in the both, however, the axonal (Ax) degenerations are stronger in the caudal segment than in the rostral segment. dense body (DB)

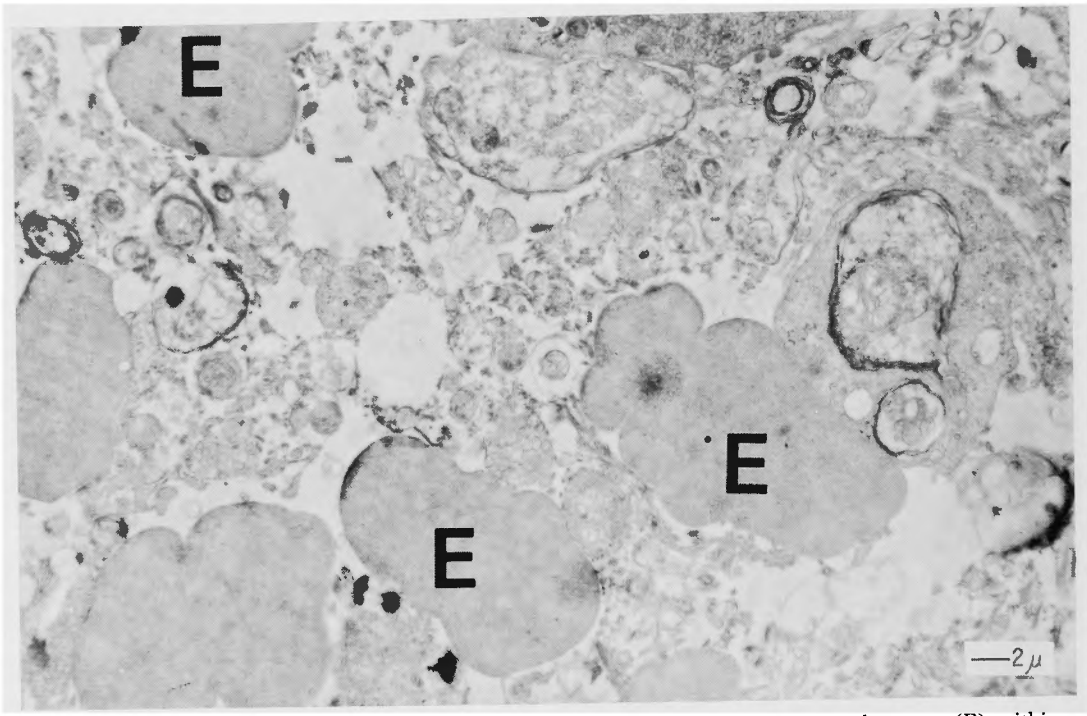


Fig. 24 Electron micrograph of the gray matter in the group IV. Numerous erythrocytes (E) within the gray matter are appeared.

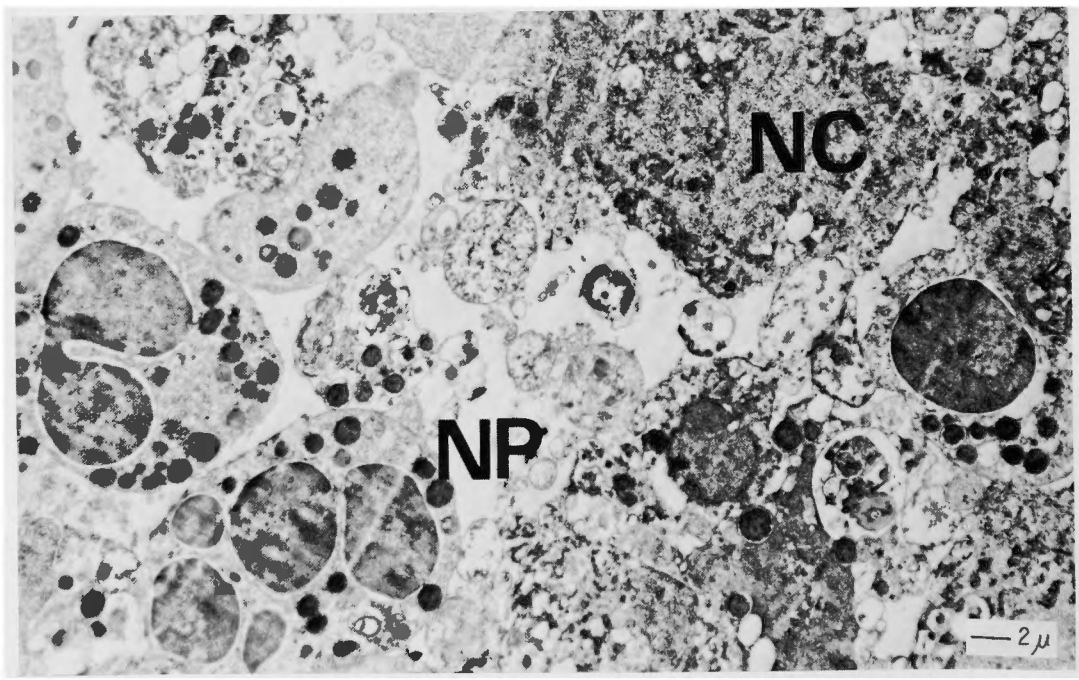


Fig. 25 Electron micrograph of the gray matter in group IV. Showing the degenerative nerve cell (NC) and the infiltration of the neutrophile (NP)

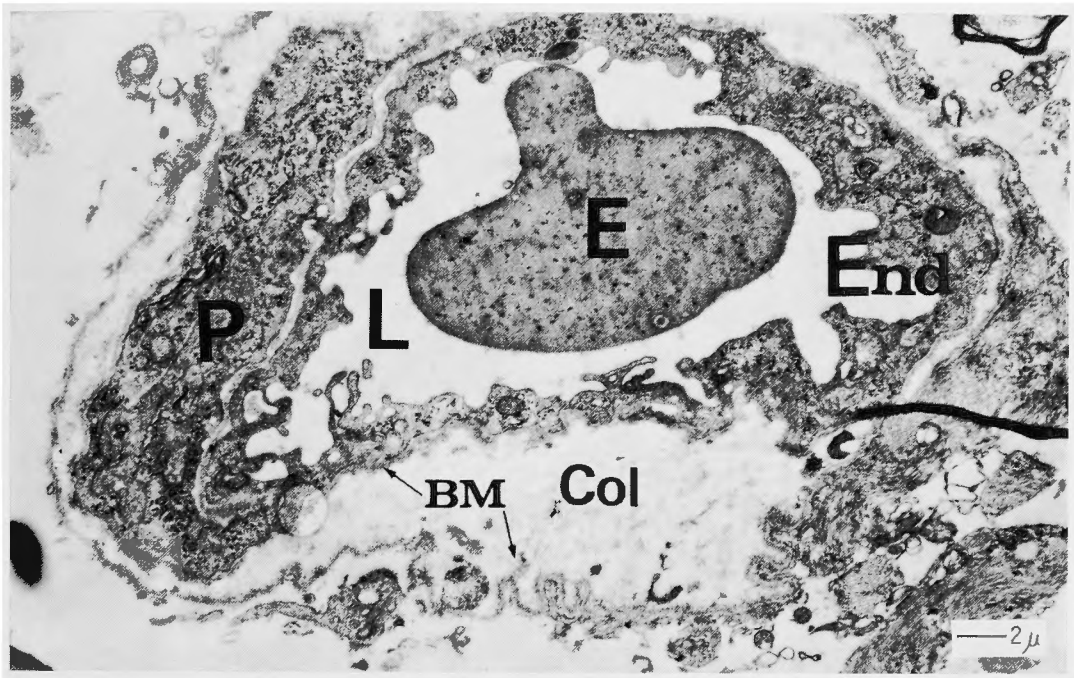


Fig. 26 Electron micrograph of the capillary in group IV. Endothelial cell (End) and Pericyte (P) are the findings of degeneration. The lumen (L) of capillary is irregular and the interstitial space is edematous.

erythrocyte (E) ; basement membrane (BM) ; collagen fibril (Col)

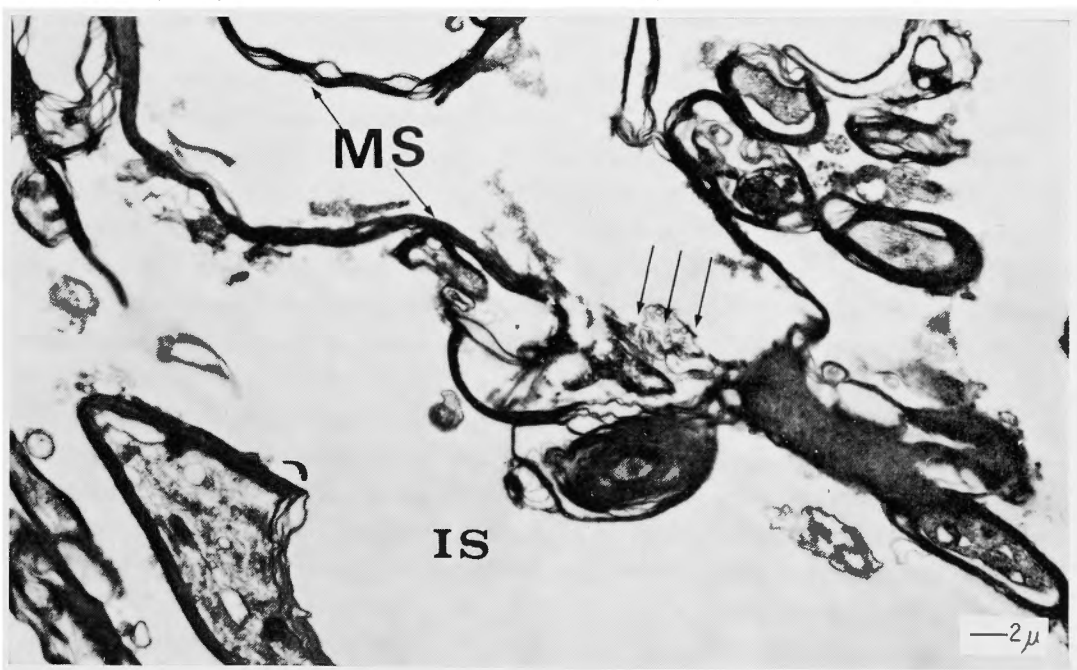


Fig. 27 Electron micrograph of the white matter in group IV. The myelin sheath (MS) are attenuated and broken (arrows). The interstitial space (IS) is greatly edematous.

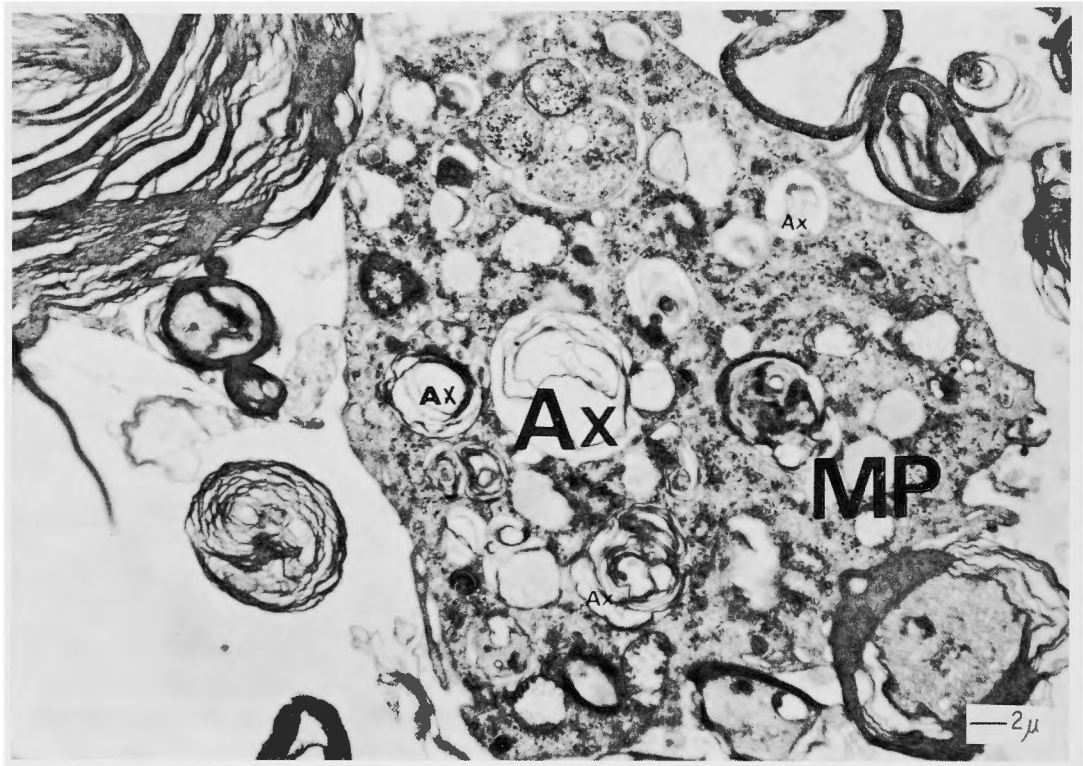


Fig. 28 Electron micrograph of the white matter in group IV. The degenerated axons (Ax) are phagocyted by a macropharge (MP).

WAGNER, et al.[40] reported the microscopic appearance of the monkey's spinal cord within 4 hours following the delivery of a direct force (300 gm-cm) sufficient to produce a transitory paraplegia. They mentioned that the main pathologic change was hemorrhagic lesion in the gray matter, this was attributed to the direct effect of the trauma on the vessels in the gray matter, with a consequent impairment of blood supply to the injured spinel cord. Further, they observed edematous changes in the affected nerve fibers such as breakage or marked attenuation of the myelin sheath and denuding of the axons[3,4].

My experimental results in group IV were similar to what they noted in spinal cord contusion.

In the myelopathy group the most striking observations were edematous changes in the microvasculature of the spinal cord and degeneration of affected nerve fibers. The main findings of edematous changes in the capillaries were vacuolation of the endothelial cells, marked narrowing of the lumina and swelling of the perivascular feet. These findings were observed more in the gray matter than in the white matter. Why the gray matter is more vulnerable is uncertain. TOMINAGA[37] reported the results of two dimensional photoelastic compression studies using cervical cord models. These were made of polyurethane rubber after measuring the dynamic intensity of human and bovine cervical cord. According to his results the distribution of the compressive stress mainly involved the central

area of the cord model. This means that the gray matter receives the greatest compressive stress in the cord.

WAGNER[40,43] also mentioned that the greater vulnerability of the vessels within the gray matter in contrast to those in the white matter may be caused by their density within the gray matter and on the abscence of firm supporting tissue.

The presence of numerous endothelial vacuoles and the swelling of endothelial cells suggested existence of ischemic condition in the cord[3]. Presumably these pathological alterations in the microvasculature were caused by decrease in blood flow to the compressed spinal cord. In all events, these findings were indicative of disturbance of the circulation in the microvasculature of the compressed spinal cord. In this way when edematous changes occur in the capillaries, it is quite possible to make vasoparalysis of the capillaries, resulting in more circulatory disturbance in the cord[19,20].

In the no deficit group the periaxonal spaces were dilated and the myelin sheaths appeared attenuated, and the degree of these changes gradually increased in order of 1,3 and 6 months after surgery. But axonal morphology was not altered.

In the myelopathy group the periaxonal spaces were markedly dilated with attenuated myelin sheaths and the axons were in various states of degeneration. These pathological changes in the myelinated nerve fibers were similar to edematous changes that were reported by LAMPERT, et al.[24] in the brains of ducklings intoxicated with isonicotinic acid hydrazide.

Some of the degenerated axons of my study also contained vesicle and dense body. These changes may be reversible since the findings were similar to that of the reactive axon or regenerating axon, as mentioned by LAMPERT[23]. The axonal degeneration in the chronic compression of the spinal cord may be related to the increase in the periaxonal fluid, which was agreed with the increase of periaxonal spaces in myelinated nerve fibers and axonal degeneration. TANI and EVANS[35] described in their studies on cerebral edema secondary to cerebral compression by an epidural balloon. This axonal degeneration due to edema may cause disturbance of the conductive pathway within the spinal cord[16,17]. On that point, ISHII and SATO, et al.[20] reported that there was slowing in the conduction velocity when the cerebral edema secondary to cerebral compression occured and the myelin lamellae were splitted.

As to the extension of the lesion within the spinal cord, DUCKER, et al.[5] reported that pathlogical changes of the spinal cord secondary to acute trauma extended from the central gray matter to the pheripheral white matter. But in my study pathological changes in the nerve fibers were the most striking at the point where the compression was applied. Spinal cord edema in the compressed segments extended rostrally and caudally, but these changes in the caudal segments were stronger than in the rostral segments, as MORIYASU and NAKAMURA[25] have reported.

These are some microangiographic and histological studies in experimental cervical myelopathy[5,6,7]. HAYAKAWA and HATTORI, et al.[14] produced experimental cervical myelo-

pathy using the same method as this study, and observed microangiographically that there was a vascular impairment in the central gray matter and the lateral funiculi of the cord, and that these impairments also extended to one or two segments above and below the site of compression. The localization of the vascular impairment was correlated almost exactly with histological evaluation of the lesions. After the decompressive operation of the cord which was made by removing of the screw, there was a correlation of improvement in both histological lesions and vascular impairment.[27] These experimental finding suggest that the damage of the cord in myelopathy is mild, and somewhat reversible. This differs from the findings observed in experimental spinal cord injury which is mainly composed of amorphos necrotic tissue and aggregated red blood cells with only a small rim of identifiable white matter[44].

Recently the pathogenesis of the cervical myelopathy regarding the pathologic findings of the patient with cervical myelopathy in cadavers was discussed[21,36,39]. KAMEYAMA[21] reported that the main pathological changes in the cadavers with cervical myelopathy were the ischemic lesions of the doughnut-like region bordered between the central and peripheral arterial system as mentioned by TURNBULL, et al.[39] In comparison of the pathological changes in the spondylotic myelopathy and compression myelopathy due to tumor, ONO[29] and OGINO[28], et al. concluded that the main pathological changes in the former were ischemic lesions due to compression over a long term and in the latter the lesions were due to venous congestion and compression.

Recent publications concerning biogenic amine in experimental spinal cord trauma was reported by OSTERHOLM[30,31] and many others[15,32]. SHIGETOMI and HATTORI, et al.[33] assayed biogenic amine in the spinal cord of the rabbits using the same method as my study. They mentioned that the experimental cervical myelopathy group had no significant changes in norepinephrine, dopamine and serotonin levels, but in the acute spinal cord injury group norepinephrine levels showed significant elevation. This fact was consistent with the author's experimental results that the edematous changes in the capillaries and affected nerve fibers were main findings in the cord.

At all events, the pathogenesis of the human cervical myelopathy is still not clear since we cannot produce an experimental model of myelopathy equal to the human cervical myelopathy under existing circumstances. But the author presumed from the experimental results that cervical myelopathy might be produced by impairment of the conductive pathway due to axonal degeneration and edematous changes of the myelin sheaths, and also by the ischemic states of the spinal cord under edematous changes of capillaries.[45,46].

Summary

1. Electron microscopic study was done in experimental cervical myelopathy using rabbits for the materials. The animals were given anterior compression of the cord and divided into three groups according to the degree of neurologic signs.

2. In the non deficit group, there were no degenerative changes in the nerve cells and

axons in the cord. Slightly edematous changes were observed in the nerve fibers and capillaries.

3. In the experimental myelopathy group, the most striking observations were edematous changes in the microvasculature and degenerative changes in the myelinated nerve fibers. Though certain nerve cells had degenerative changes, they were slight.

4. In the acute cord injury group, the main findings were hemorrhage in the gray matter. Also severe damage was observed in the myelinated nerve fibers.

5. It was presumed from author's experimental results that cervical myelopathy might be produced by impairment of the conductive pathway due to axonal degeneration and edemotous changes of the myelin sheaths, and also by the ischemic state of the spinal cord under edematous changes of capillaries.

Acknowledgement

The author wishes to express grateful acknowlegement to Prof. Dr. SUSUMU HAATTORI, Department of Orthopaedic Surgery, Yamaguchi University School of Medicine for his helpful guidance and encouragement, to Prof. Dr. FUMIYA UCHINO, First Department of Pathology, Yamaguchi University School of Medicine for his helpful advice, to associate Prof. Dr. SHINYA KAWAI, Department of Orthopaedic Surgery, Yamaguchi University School of Medicine for his very careful suggestion and revision and to all of my colleague in the Department of Orthopaedic Surgery.

This work was supported by Grant-in-Aid for Scientific Research of the Ministry of Education Science and Culture. The results were presented in part at the 47 th Central Japan Meeting of Orthopedic and Traumatic Surgery, and at the 50 th Annual Meeting of the Japanese Orthopedic Association.

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和文抄録

実験的頸椎ミエロパチーの電子顕微鏡的研究

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山　口　芳　英

頸部脊椎骨軟骨症の myelopathy の病態を追求する目的で家兎頸椎に慢性圧迫を加え，その病理組織学的変化を透過型電子顕微鏡で観察した．静脈麻酔下に成熟家兎の第4-5頸椎椎間板に前方進入法により徐々に螺子を刺入し，頸髄を前方から圧迫した．圧迫の程度はレ線にて計測し，手術後の臨床症状より以下の群に分類した．即ち，1）急性脊髄損傷例（以下脊損例）：手術直後より歩行不能，四肢麻痺，直腸膀胱障害を認め，回復することなく経過した群で，5羽がこれに属する．2）実験的ミエロパチー例（以下M例）：手術翌日より何等神経症状を呈することなく一定期間経過した後，痙性歩行あるいは不安定歩行，四肢運動障害，深部腱反射亢進等の脊髄症状を認めた群で，圧迫率31～50％の15羽中6羽に手術後2～6週してM例を認めた．3）無症状例：6カ月の観察期間中，何等神経症状を呈さずに経過した群で，28羽がこれに属する．非手術例10羽を正常例とした．無症状例は1カ月，3カ月，6カ月の時点で，M例・脊損例は症状発生後数日以内に3％ Glutalaldehyde にて灌流固定後，脊髄を摘出し，細切して1％ Glutalaldehyde，1％ OsO_4 の二重固定，Epon 812 の包埋，酢酸ウラニール・Pb の二重染色を行ない圧迫髄節及びその上・下髄節の病理組織学的変化を電子顕微鏡にて観察した．正常例の灰白質では神経細胞とそれらの突起，白質では神経線維が互いに密に充塡している．毛細血管内壁には内被細胞があり，これを囲んで二層の基底膜があり，その外

側には astrocyte の突起が接している．無症状群では毛細血管基底膜の拡大，髄鞘の分離を認め，圧迫期間が長い程，その変化も強かったが，神経細胞に変化は認めなかった．M例の神経細胞は変性所見が認められ，axon の空胞変性，periaxonal space の著明な拡大，ミトコンドリアの変性，毛細血管内腔の狭小化，基底膜の著明な拡大，collagen fibril の増生，astrocyte 突起の腫大を認めたが，灰白質の出血は認めなかった．脊損例では灰白質の壊死，出血，間質の浮腫，髄鞘の破壊，毛細血管内腔の著明な狭小化を認めた．上・下髄節での組織学的所見では神経細胞，血管の所見に大差は認めなかったが，神経線維の変化は頭側よりも尾側の変化が強かった．Dorhrmann 等の急性圧迫実験によると，主病変は灰白質の出血とそれによる blood supply の障害と浮腫による axon の変性であると報告しているが，慢性圧迫の場合は灰白質の出血は認めず，神経細胞の変化は軽度であり，毛細血管の浮腫性変化と神経線維の変性が著明であった．以上の電子顕微鏡所見からすれば，実験的ミエロパチーの場合には圧迫によって，神経線維の浮腫や変性のために vasoparalysis の状態となり，これが脊髄の循環障害を招来し，ミエロパチー様症状を惹起する一因ではないかと推論する．